Iterative feedback tuning of proportional-integral controller parameters for adaptive deep brain stimulation

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***Abstract*—Deep brain stimulation (DBS) is a well-established method for symptomatic treatment of Parkinson's disease and essential tremor. Adaptive deep brain stimulation has the potential to surpass the performance of conventional DBS, providing more accurate symptom suppression, better control of stimulation-induced side effects, and longer battery life. While multiple controllers have been proposed and successfully tested in computational models as well as in patients, even the simple methods still require parameter tuning and currently there is there is no known optimal way of setting the parameters of these controllers. In this work, we have applied an iterative feedback tuning (IFT) method to set proportional-integral controller parameters to values that minimize a specific performance metric. The metric used is based on the residual local field potential (LFP) beta power and the stimulation intensity, rewarding maximum beta suppression with minimal stimulation intensity. We have tested this method in a computational model of parkinsonian basal ganglia, capable of modelling the pathological beta activity and simulating the LFP. We have shown that the controller parameters are updated in accordance with the predefined goals and that the behaviour of the controller is dependent on the relative importance ascribed to the beta power and the stimulation intensity.**

***Index Terms*—deep brain stimulation, adaptive DBS, iterative feedback tuning**

I. Introduction

Closed-loop, or adaptive deep brain stimulation (aDBS) has been proposed as an approach to augment the efficacy of continuous DBS, promising better control of disease symptoms, longer battery life and reduced risk of stimulation-induced side effects. In contrast to conventional DBS in which stimulation parameters remain fixed over time, in aDBS the stimulation parameters (most commonly amplitude and frequency) are updated in real time, based on the measurement of a biomarker that provides information on the patient's condition in order to better fit the current needs of the patient.

While aDBS is not yet used in clinical practice, a number of studies have been conducted to trial aDBS over short durations in patients with Parkinson's disease. The methods used have been based on the basal ganglia β-band (13-30 Hz) activity [1], [2], which correlates with the parkinsonian symptoms of bradykinesia and rigidity [3], or tremor power measured with a wrist-mounted accelerometer [4]. The approaches tested to date fall into three broad categories: *on-off control*, where the stimulation is applied when the biomarker exceeds a threshold value [1], [5]; *proportional control*, where the stimulation amplitude is proportional to the value of the biomarker [2], [6]; and *ramping/dual-threshold control*, where the amplitude is adjusted with a preset rate of change, depending on value of the biomarker in relation to two thresholds [4], [7].

In addition to these clinically tested methods, computational studies of aDBS for Parkinson's disease have explored a variety of stimulation approaches. Unconstrained by the limitations of the implanted devices, these methods range from simple proportional control [8], to computationally expensive Bayesian optimisation algorithms [9], [10].

The proposed closed-loop methods obviate the need to directly set the stimulation parameters but introduce another set of parameters, the choice of which influences the performance of the control setup. A good example of this is the case of the proportional-integral (PI) controller, a variant of the proportional-integral-derivative (PID) controller. The PI controller can successfully be used to suppress pathological β oscillations in computational models of cortico-basal ganglia loop [11] but inappropriately chosen parameters will result in either unsatisfactory suppression or overstimulation. To address this issue, several methods have been proposed in a "dual-loop" paradigm, where adaptation of the stimulation parameters is performed by an internal PI controller, while the parameters of the PI controller are updated by an external controller, based on a chosen performance metric [9], [12].

In this work we apply iterative feedback tuning (IFT), to optimize the parameters for PI control of DBS. IFT was proposed in [13] for linear systems and extended to nonlinear systems in [14]. It provides a systematic way based on gradient estimation to adjust parameters of any linear controller, using signals measured from the system during stimulation to minimize a predefined cost function, and is simple enough to implement in embedded devices [15]. We test the implementation of IFT in

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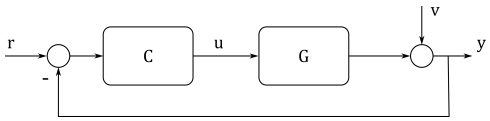

Fig. 1. The closed loop system.

a computational model of the cortico-basal ganglia loop, that exhibits pathological β oscillations, similar to those present in patients suffering from Parkinson's disease, and show that the controller parameters are updated in accordance with the predefined control objectives.

II. Methods

The cortico-basal ganglia model and the controller are connected in a closed loop (Fig.1). The IFT PI controller C is described in detail in Section II-A and G is the model described in Section II-B. The signal r is the controller reference signal, u is the controller output, v is the disturbance and y is the system output, i.e. the value of the biomarker.

A. Iterative feedback tuning

The objective is to minimize a cost function

$$J(\rho) = \frac{1}{2N} E\left[\sum_{t=1}^{N} \tilde{y}[t;\rho]^2 + \lambda u[t;\rho]^2\right], \tag{1}$$

where ρ encodes the parameters of the controller, t represents each discrete time point, $u[t]$ is the controller output (stimulation amplitude), $\tilde{y}[t] = y[t] - r[t]$ for the measured output of the system $y[t]$ and the reference signal $r[t]$, $N \in \mathbb{N}$ is the signal length, and $\lambda \in \mathbb{R}_{\geq 0}$ is a scaling parameter. This function represents a weighted sum of the mean squared errors of the biomarker and the control input.

If $J(\rho_i)$ was known for a given parameter vector ρ_i, we could find a local optimum by iterating

$$\rho_{i+1} = \rho_i - \gamma_i R_i^{-1} \frac{\partial J}{\partial \rho}(\rho_i), \tag{2}$$

where $\gamma_i > 0$, and R_i is a positive-definite matrix for all $i \in \mathbb{N}$. Since $J(\rho_i)$ is not known a priori, it has to be estimated, as shown in [16]:

$$\begin{aligned}\text{est}\left[\frac{\partial J}{\partial \rho}(\rho_i)\right] = \frac{1}{N}\sum_{t=1}^{N}\Bigg(&\tilde{y}[t;\rho_i]\text{est}\left[\frac{\partial y}{\partial \rho}[t;\rho_i]\right] \\ &+ \lambda u[t;\rho_i]\text{est}\left[\frac{\partial u}{\partial \rho}[t;\rho_i]\right]\Bigg),\end{aligned} \tag{3}$$

where

$$\text{est}\left[\frac{\partial y}{\partial \rho}(\rho_i)\right] = \frac{1}{C(\rho_i)}\frac{\partial C}{\partial \rho}(\rho_i) y_2(\rho_i) \tag{4}$$

and

$$\text{est}\left[\frac{\partial u}{\partial \rho}(\rho_i)\right] = \frac{1}{C(\rho_i)}\frac{\partial C}{\partial \rho}(\rho_i) u_2(\rho_i). \tag{5}$$

The controller C is a PI controller, defined in the z-domain with backward Euler approximation as

$$C(z;\rho) = K_p\left[1 + \frac{T_s}{T_i(1-z^{-1})}\right], \tag{6}$$

where $\rho = (K_p, T_i)^T$ is a parameter vector with $K_p, T_i \in \mathbb{R}_{\geq 0}$ and $T_s > 0$ is the controller sampling time. Next, we compute the transfer functions needed for the estimators (4) and (5)

$$\frac{1}{C}\frac{\partial C}{\partial \rho}(\rho) = \begin{pmatrix} \dfrac{1}{K_p} \\ \dfrac{-T_s z}{T_i(T_i z - T_i + T_s z)} \end{pmatrix}. \tag{7}$$

Following [16], the signals y_2 and u_2 are obtained as follows:

- set the reference signal to the desired value $r = y_d$ and record N samples of the controller output signal u_1 and the system output $y_1 = \tilde{y} = y - r$,
- set $r = y_1$ and record N samples of the controller output u_2 and system output y_2,
- use the measured signals y_1, y_2, u_1, u_2 in (3)-(5) to obtain the estimate of the gradient of the cost function J,
- update the controller parameters as in (2).

This process can be performed for a predefined number of iterations, until a convergence criterion is met, or indefinitely, depending on the design goals. For the purposes of the simulation, the transfer function (7) was expressed in a difference equation form and applied to equations (4)-(5).

B. Computational model of cortico-basal ganglia loop

To test the application of IFT to identify controller parameters suitable for suppression of pathological oscillations in the basal ganglia, we used a computational model, proposed in [11]. This model exhibits β oscillations akin to those observed in parkinsonian patients, and simulates the local field potentials (LFP) as well as DBS stimulation that suppresses the β activity. The model is implemented in Python using PyNN and runs on the NEURON simulator with 0.5 ms time step.

The model was updated to utilize NEURON and PyNN's parallelization capabilities. The simulations presented in this paper were run with 12 threads.

The controller updates the stimulation parameters every $T_s = 20$ ms based on the system output y and the reference signal r. The output y is obtained by bandpass-filtering the LFP in the high β (21-29 Hz) range (4th order Chebyshev Type I filter, 0.5 dB ripple) and calculating the average rectified value of the filtered signal over the 2000 ms preceding the controller call.

III. Results

A. Estimate of the cost function J

To obtain an approximate value of the cost function J for any given set of parameters, we ran the simulation with a PI controller with fixed K_p and T_i for a range of values between 0 and 2. The simulation was first advanced 6 s to allow the system settle to the steady state. The PI controller was then applied to the model for 12 s and we estimated the mean square error of the β activity $\tilde{y}^2$ and the square of the stimulation amplitude u^2 over the final 6 s of the simulation.

The performance of the model for different combinations of controller parameters are presented in Fig.2. The beta power

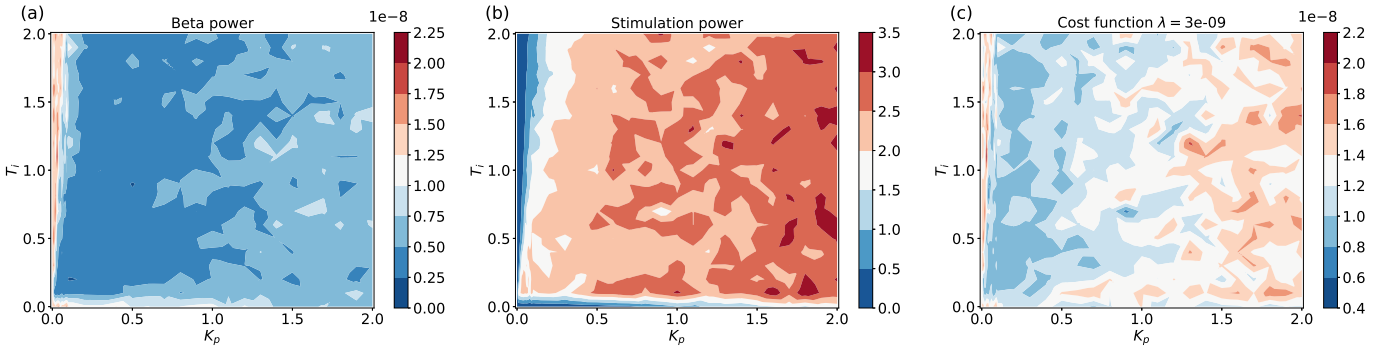

Fig. 2. Components of the cost function J estimated from simulations with fixed-parameter PI controller. The simulations were run for 6 seconds to reach the steady state and then for 12 seconds with the controller on. The values for every parameter pair were obtained by averaging over the final 6 seconds of the simulation and then the plots were created by linearly interpolating between the obtained values. **(a)** Mean square error of the beta amplitude, corresponding to the y^2 term. **(b)** Squared stimulation amplitude, corresponding to the u^2 term. **(c)** Cost $J = \sum_i y[i]^2 + \lambda u[i]^2$ with $\lambda = 3 \times 10^{-9}$.

(Fig.2a) was generally well-suppressed with sufficiently high values of K_p and T_i. On the other hand, the stimulation power (Fig.2b) increased steeply with increasing proportional gain K_p and was reduced by increasing the integral time constant T_i. Since the two terms have opposing effects, it is clear that the choice of the λ parameter is critical in determining the behaviour of the controller. A cost function with a high λ will push the controller towards lower K_p values to minimize the stimulation amplitude, while a low λ will cause K_p to increase to achieve better suppression of β power.

Fig.2c presents the cost function with $\lambda = 3 \times 10^{-}9$.

B. Adaptation of parameters through iterative feedback tuning

We then applied the IFT controller, described in Section II-A, to the same model with the same initial conditions to tune the PI controller parameters automatically.

The results of running the IFT controller for two different values of λ are shown in Fig.3. The simulations were run for 60 s, with the signal length $N = 125$, corresponding to 2.5 s, and $\gamma = 0.05$. The background shows the approximated cost function for a given value of λ and the arrows represent the change of the PI controller parameters.

When $\lambda = 0$ (Fig.3a), the algorithm minimizes the β oscillation magnitude, so it moved towards the higher values of K_p. Initial controller parameter values of $K_p = 0.05$, $T_i = 1.30$ were updated to the final values of $K_p = 0.96, T_i = 1.29$.

When $\lambda = 1$ (Fig.3b) and the cost function J is dominated by the u^2 part, representing the stimulation amplitude, the algorithm increased the value of T_i and reduced the value of K_p. Initial values for this simulation were $K_p = 1.00$, $T_i = 0.20$ and the final values were $K_p = 0.17, T_i = 1.20$.

IV. Discussion

A PI controller with well-tuned parameters is capable of reducing the β power in models of parkinsonian brain activity, while also reducing the stimulation intensity compared to continuous stimulation. However, identifying effective controller parameters is a nontrivial problem.

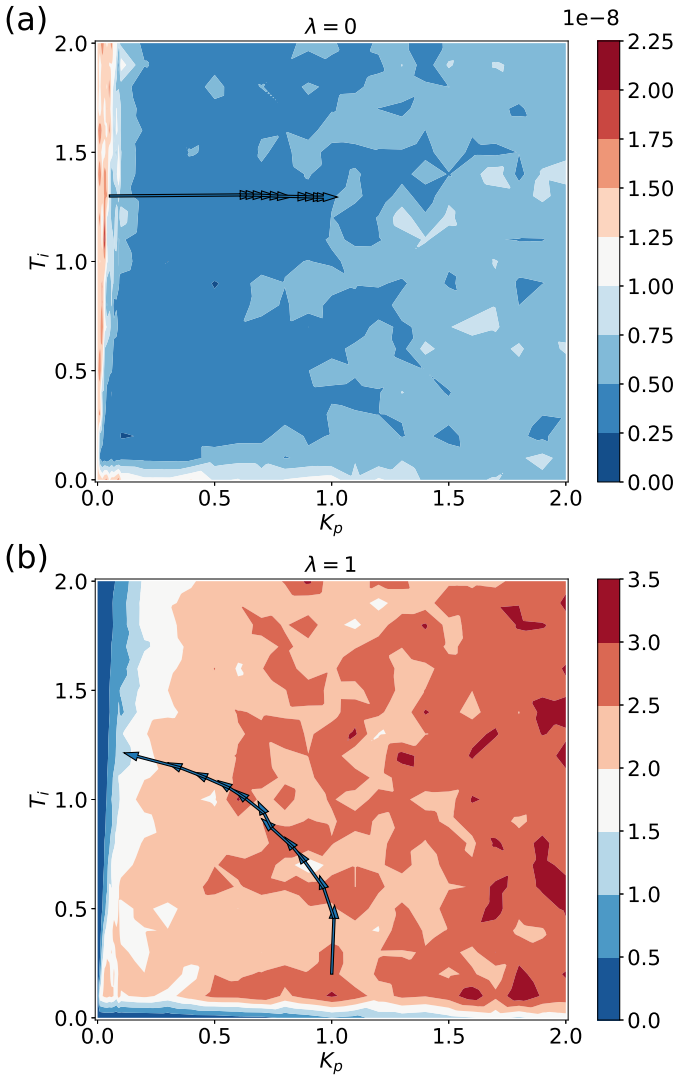

Fig. 3. Results of IFT application to a PI controller with two different λ values. **(a)** When $\lambda = 0$, the parameters are increased in the direction of higher K_p, to maximize beta suppression. **(b)** When $\lambda = 1$, the IFT process pushes the parameters towards higher values of T_i and lower values of K_p to minimize the stimulation power.

Here an iterative method is proposed to tune the parameters in accordance with any specified cost function. The cost function used here is based on the mean square error of the β amplitude and stimulation amplitude. These two parts of the cost function introduce competing requirements on the values of the controller parameters. The suppression of β requires higher values of K_p and lower values of T_i, while the reduction of stimulation intensity requires lower values of K_p and higher values of T_i. The method proposed here is capable of finding an effective set of parameters, given those competing constraints, with the final value depending on the relative weighting given to the two components.

Methods that automatically adjust the controller parameters, such as the IFT presented here, have the potential to simplify the implementation and deployment of aDBS, replacing a set of parameters that is hard to tune (the gain and time constant of the PI controller) by a set of parameters with a more intuitive meaning (relative importance of β intensity and stimulation intensity and the signal length). Moreover, these methods have the potential to respond to changes in the underlying activity, as the disease progresses or the electrical impedance of the tissue surrounding the electrode changes, altering the fitness landscape and diminishing the efficacy of DBS treatment.

Methods of low computational complexity, like the IFT, could be implemented in existing hardware, as opposed to methods relying on machine learning to generate the estimate of the cost function [10]. While the computational burden can be offloaded to the cloud and the parameter update can be performed remotely, such solutions have additional requirements in terms of device connectivity, which additionally raises issues related to privacy and security.

While IFT performs well for the conditions examined, further research is required not only to better understand the effect of IFT parameters on controller performance but also to compare this approach with other proposed aDBS methods, such as model-adaptive control [17]. Such comparative studies would serve to illuminate the relative strengths and weaknesses of these methods and their domains of applicability.

Moreover, the presented model does not include any information about the muscle activity, the non-motor effects of stimulation and the stimulation-induced side effects. A simple PI controller, even with the advantage of IFT, would not be able to address all these issues.

There is a gap between the simple methods of brain stimulation, that have been tested in clinical trials of aDBS, and more advanced methods proposed in computational studies. The ability of IFT to adjust the controller parameters based on a prescribed cost function obviates the need for costly and time-consuming parameter tuning. Moreover, its low computational complexity makes it suitable for testing in existing hardware, allowing for significant increase in capabilities of aDBS devices without significant technological advances.

REFERENCES

[1] S. Little, A. Pogosyan, S. Neal, B. Zavala, L. Zrinzo, M. Hariz, T. Foltynie, P. Limousin, K. Ashkan, J. FitzGerald, A. L. Green, T. Z. Aziz, and P. Brown, "Adaptive deep brain stimulation in advanced Parkinson disease," *Annals of Neurology*, vol. 74, no. 3, pp. 449–457, Sep. 2013.

[2] M. Rosa, M. Arlotti, S. Marceglia, G. Ardolino, F. Cogiamanian, A. Di Fonzo, P. Rampini, and A. Priori, "Adaptive deep brain stimulation in patients with Parkinson's disease: phase II clinical trial preliminary results," *Journal of the Neurological Sciences*, vol. 357, pp. E285–E285, Oct. 2015.

[3] C. Hammond, H. Bergman, and P. Brown, "Pathological synchronization in Parkinson's disease: networks, models and treatments." *Trends in neurosciences*, vol. 30, no. 7, pp. 357–64, Jul. 2007.

[4] M. Malekmohammadi, J. Herron, A. Velisar, Z. Blumenfeld, M. H. Trager, H. J. Chizeck, and H. Brontë-Stewart, "Kinematic Adaptive Deep Brain Stimulation for Resting Tremor in Parkinson's Disease," *Movement Disorders*, vol. 31, no. 3, pp. 426–428, Mar. 2016.

[5] S. Little, M. Beudel, L. Zrinzo, T. Foltynie, P. Limousin, M. Hariz, S. Neal, B. Cheeran, H. Cagnan, J. Gratwicke, T. Z. Aziz, A. Pogosyan, and P. Brown, "Bilateral adaptive deep brain stimulation is effective in Parkinson's disease." *Journal of neurology, neurosurgery, and psychiatry*, vol. 87, no. 7, pp. 717–21, 2016.

[6] M. Arlotti, S. Marceglia, G. Foffani, J. Volkmann, A. M. Lozano, E. Moro, F. Cogiamanian, M. Prenassi, T. Bocci, F. Cortese, P. Rampini, S. Barbieri, and A. Priori, "Eight-hours adaptive deep brain stimulation in patients with Parkinson disease," *Neurology*, vol. 90, pp. e971–e976, 2018.

[7] A. Velisar, J. Syrkin-Nikolau, Z. Blumenfeld, M. H. Trager, M. F. Afzal, V. Prabhakar, and H. Bronte-Stewart, "Dual threshold neural closed loop deep brain stimulation in Parkinson disease patients," *Brain Stimulation*, vol. 12, no. 4, pp. 868–876, 2019.

[8] W. Pasillas-Lepine, I. Haidar, A. Chaillet, and E. Panteley, "Closed-loop deep brain stimulation based on firing-rate regulation," Nov. 2013.

[9] L. L. Grado, M. D. Johnson, and T. I. Netoff, "Bayesian adaptive dual control of deep brain stimulation in a computational model of Parkinson's disease," *PLOS Computational Biology*, vol. 14, no. 12, p. e1006606, Dec. 2018.

[10] P. Sarikhani, H.-l. Hsu, and B. Mahmoudi, "Automated Tuning of Closed-loop Neuromodulation Control Systems using Bayesian Optimization," 2022, pp. 1763–1766.

[11] J. E. Fleming, E. Dunn, and M. M. Lowery, "Simulation of Closed-Loop Deep Brain Stimulation Control Schemes for Suppression of Pathological Beta Oscillations in Parkinson's Disease," *Frontiers in Neuroscience*, vol. 14, p. 166, Mar. 2020.

[12] J. Orłowski, A. Chaillet, A. Destexhe, and M. Sigalotti, "Adaptive control of Lipschitz time-delay systems by sigma modification with application to neuronal population dynamics," *Systems & Control Letters*, vol. 159, p. 105082, Jan. 2022.

[13] H. Hjalmarsson, S. Gunnarsson, and M. Gevers, "A convergent iterative restricted complexity control design scheme," in *Proceedings of 1994 33rd IEEE Conference on Decision and Control*, vol. 2, Dec. 1994, pp. 1735–1740 vol.2.

[14] H. Hjalmarsson, "Control of nonlinear systems using iterative feedback tuning," in *Proceedings of the 1998 American Control Conference. ACC (IEEE Cat. No.98CH36207)*, vol. 4, Jun. 1998, pp. 2083–2087 vol.4.

[15] G. Himunzowa, "Investigations into implementation of an iterative feedback tuning algorithm into microcontroller," Master's thesis, University of Cape Town, 2008, accepted: 2014-07-31T10:56:57Z.

[16] H. Hjalmarsson, M. Gevers, S. Gunnarsson, and O. Lequin, "Iterative feedback tuning: theory and applications," *IEEE Control Systems Magazine*, vol. 18, no. 4, pp. 26–41, Aug. 1998.

[17] S. Santaniello, G. Fiengo, L. Glielmo, and W. M. Grill, "Closed-Loop Control of Deep Brain Stimulation: A Simulation Study," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 19, no. 1, pp. 15–24, Feb. 2011.